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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT

PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/265,606

Applicant(s)

ZIMMERMANN ET AL.

Examiner

Nancy Ogihara

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 5 and 16-19 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 5, 16-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) ____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Response to Amendment

The examiner acknowledges receipt of the Declaration and the Amendment under 37 CFR 1.111, dated 7/25/00. The Amendment, amending claims 5, 16, 17, and 19, is acknowledged. Claims pending and under consideration are claims 5 and 16-19.

Objections Withdrawn

In view of Applicant's Amendments, the following objection is withdrawn.

The objection to the specification due to the lack of the necessary references to prior applications to which applicant seeks priority, is withdrawn in view of Applicant's Amendment filed 7/25/00.

Rejections Withdrawn

In view of Applicant's Amendments, the following rejections are withdrawn.

The rejection of claims 5 under 35 U.S.C 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (pages 4-5 of the previous Office Action), is withdrawn in view of Applicant's arguments as stated in the Amendment filed 7/25/00.

The rejection of claim 5 under 35 U.S.C 112, second paragraph, as being indefinite in the recitation of the term "FAP α catalytic domain" (page 4 of the previous Office Action), is withdrawn in view of Applicant's clarification that residues 621-737 constitute the catalytic domain, as stated in the Amendment filed 7/25/00.

The rejection of claims 16, 17, and 19 under 35 U.S.C 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (page 5 of the previous Office Action), is withdrawn in view of Applicant's election to present the invention in different terms (i.e. "non-FAP α " protein, and "fusion") as stated in the Amendment filed 7/25/00.

Rejections Maintained

The rejection of claims 5 and 16-19 under 35 U.S.C. 101, as lacking patentable utility (page 3 of the previous Office Action) is maintained in view of Applicant's arguments in the Amendment filed 7/25/00.

Applicant argues that the claimed proteins are of sufficient size that they can function as immunogens for determining expression of FAP α in a sample.

As set forth in the previous office action, the specification has not shown that upon removing the FAP α catalytic domain from the full length FAP α protein, the FAP α catalytic domain is functional or has activity as an independent entity separate from the original full length folded protein. Thus, the claimed invention (i.e. fusion proteins) consisting of the FAP α catalytic domain and non-FAP α proteins also have not been shown to be functional or to have activity, and therefore, lacks utility because there is no asserted utility, or well-established utility, other than for further research.

The specifications disclose that the FAP α protein can be used for diagnostics as certain tumor cells are positive for FAP α expression (see page 4, lines 6-17). However, the use of the claimed FAP α catalytic domain as an immunogen is speculative, as the catalytic domain, *per se*, is commonly not available on the surface of a protein, and therefore not likely to be immunogenic. Thus, the catalytic domain would not carry with it the diagnostic utility of the entire full-length FAP α protein.

The rejection of claims 5 and 16-19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is maintained in view of Applicant's Amendment filed 7/25/00.

Applicant argues that FAP α and DPPIV have highly conserved catalytic domains (page 12 and 13) and that Ogata *et al.* (Biochemistry, vol. 31, pp. 2582-2587, 1992) have shown that the DPPIV catalytic domain is active when it stands apart from the entire DPPIV molecule. Applicant further argues that one of ordinary skill in the art would conclude that the catalytic domain of FAP α would also have activity in view of the teachings related to DPPIV.

While there may be sequence similarity between FAP α and DPPIV catalytic domains (as shown in Table 2, page 13), the sequences shown in the table cannot predictably be expected to fold into their proper three-dimensional configuration required for activity, absent the remaining amino

Art Unit: 1631

acid residues of the full-length protein. One of skill in the art would need to identify which of the remaining residues are necessary and sufficient to provide the structural scaffold necessary to form a functional FAP α catalytic domain separate from the remaining full-length protein. It should be noted that the specification discloses that FAP α has 9 conserved cysteines (see page 12, lines 20-21), most of which likely form disulfide bonds which in turn would be critical for structure and function of the catalytic domain. Furthermore, Ogata *et al.* have only described the active site residues of DPPIV (see title), and Ogata *et al.* did not show that the DPPIV catalytic domain was active when it stands apart from the entire DPPIV molecule. The 109 kDa active protein isolated by Ogata *et al.* was disclosed to be the full intact protein (see page 2584, 1st paragraph of Results, and Methods). Although FAP α and DPPIV may have similarity in their sequences, FAP α has a differing sequence from DPPIV, and therefore differing structure and differing function that cannot be predicted by knowledge of the catalytic residues of DPPIV. Geysen *et al.* (J. of Molecular Recognition, vol. 1, pp. 32-40, 1988) have shown that conservative substitutions do not necessarily correlate with a protein's ability to maintain function, such as protein-protein interactions. Even a single amino acid change in a protein antigen, including replacement with those with similar character, can be disallowed (i.e. alter or abolish function) (see page 38, 2nd paragraph). In view of all of the above, it is determined that it would require undue experimentation of one of skill in the art to make and/or use the invention as claimed.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from

Art Unit: 1631

the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Ogihara whose telephone number is (703) 308-9363. The examiner can be reached Monday-Friday from 8:30-6:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Michael Woodward can be reached at (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1631 by facsimile transmission. Papers should be faxed to Group 1631 via the PTO Fax Center located in Crystal Park I. The faxing of such papers must conform with the notice published in the Official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Nancy Ogihara
August 22, 2000

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER